An Evaluation of Pharmacy Data for Surveillance of Gastrointestinal and Respiratory Outbreaks

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ESSENCE

Electronic **S**urveillance **S**ystem for the **E**arly **N**otification of **C**ommunity-based **E**pidemics

INTRODUCTION

- **A U.S. Department of Defense (DoD) system**
- **Designed to detect infectious disease outbreaks**
- **Serves military active duty members, their beneficiaries, and retirees**
- **Uses mainly ICD-9-CM codes from outpatient visits**
- **Delay of 1- 4 days from patient visit date to data capture date by ESSENCE**

Pharmacy Data Transaction Service (PDTS)

- Developed by the DoD **P**harmaco**e**conomic **C**enter (PEC) program, managed by WebMD
- Data repository for prescriptions filled by beneficiaries of the military health system
- Approx. 61.1 million prescriptions filled annually[1]
  - 82% of prescriptions from MTFs (n=587)
  - 18% from:
    - Tricare Managed Care Support Contractors Network pharmacies (n=50,000)
    - National Mail Order Pharmacy (n=1)

ESSENCE

Update every 24 hours

PDTS

Tricare pharmacy transactions

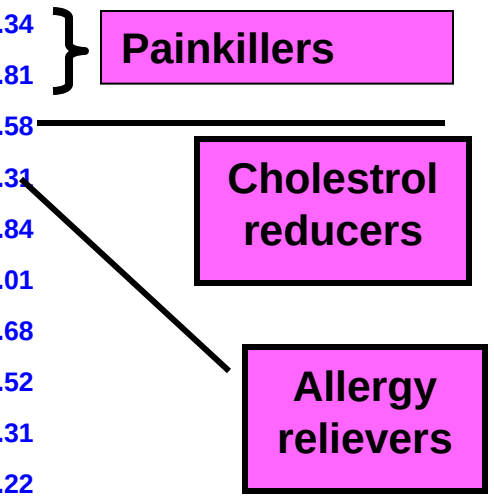
3.2 seconds

PDTS Fields

- **The PDTS formulary and standards maintained through WebMD's subscription to the American Hospital Formulary Service (AHFS), the National Council for Prescription Drug Programs (NCPDP), and First Data Bank, Inc.**
- **Medication id fields in PDTS**
  - Drug name (Label)
  - Therapeutic class number (GCN)
  - Therapeutic class code (GC3)
  - Other
- **Previous study by Scott Eader et al. using ESSENCE data for the DC metropolitan area**
  - Significant positive correlation between outpatient visit and PDTS data for GC3 codes identified for Respiratory (RESP) and gastrointestinal (GI) syndromes
- **GC3: developed by First Data Bank, Inc.**
  - 3 characters (alpha, numeric, alpha)
    - organ system, pharmacological class, specific therapeutic class, respectively

PDTS
Commonly filled medications, 2003

GC3	DESCRIPTION	COUNT	PERCENT
S2B	NSAIDS, CYCLOOXYGENASE INHIBITOR - TYPE	5603369	6.34
H3A	ANALGESICS,NARCOTICS	4256802	4.81
M4E	LIPOTROPICS	4049267	4.58
Z2A	ANTIHISTAMINES	3812841	4.31
D4K	GASTRIC ACID SECRETION REDUCERS	3395463	3.84
A4D	HYPOTENSIVES, ACE INHIBITORS	2659102	3.01
J7C	BETA-ADRENERGIC BLOCKING AGENTS	2373543	2.68
H2S	SELECTIVE SEROTONIN REUPTAKE INHIBITOR (SSRIS)	2230604	2.52
W1A	PENICILLINS	2039720	2.31
A9A	CALCIUM CHANNEL BLOCKING AGENTS	1966936	2.22
P3A	THYROID HORMONES	1700412	1.92
B3J	EXPECTORANTS	1654859	1.87
J5D	BETA-ADRENERGIC AGENTS	1557748	1.76
Q7P	NASAL ANTI-INFLAMMATORY STEROIDS	1420677	1.61
H2F	ANTI-ANXIETY DRUGS	1311393	1.48
H4B	ANTICONVULSANTS	1299466	1.47
P5A	GLUCOCORTICOIDS	1265605	1.43
R1F	THIAZIDE AND RELATED DIURETICS	1247417	1.41
W1D	MACROLIDES	1242950	1.41
A4F	HYPOTENSIVES,ANGIOTENSIN RECEPTOR ANTAGONIST	1223731	1.38



STUDY OBJECTIVES

1) Determine medications commonly prescribed for GI and RESP syndromes during outbreaks

2) Examine trends in daily counts of medications filled for GI, RESP, Asthma visits during outbreaks

3) Conduct retrospective surveillance on drug groups that correlated with GI and RESP outpatient visits during outbreaks

METHODS

- List compiled of known GI and RESP outbreaks
- Commonly prescribed non-refill medications identified for each outbreak
  - By linking ambulatory and pharmacy data by date of visit/prescription written and unique encrypted identifiers common to both data sets
- Trends in medications filled and GI/Resp visits investigated during outbreaks
  - Moving 7-day averages of daily counts

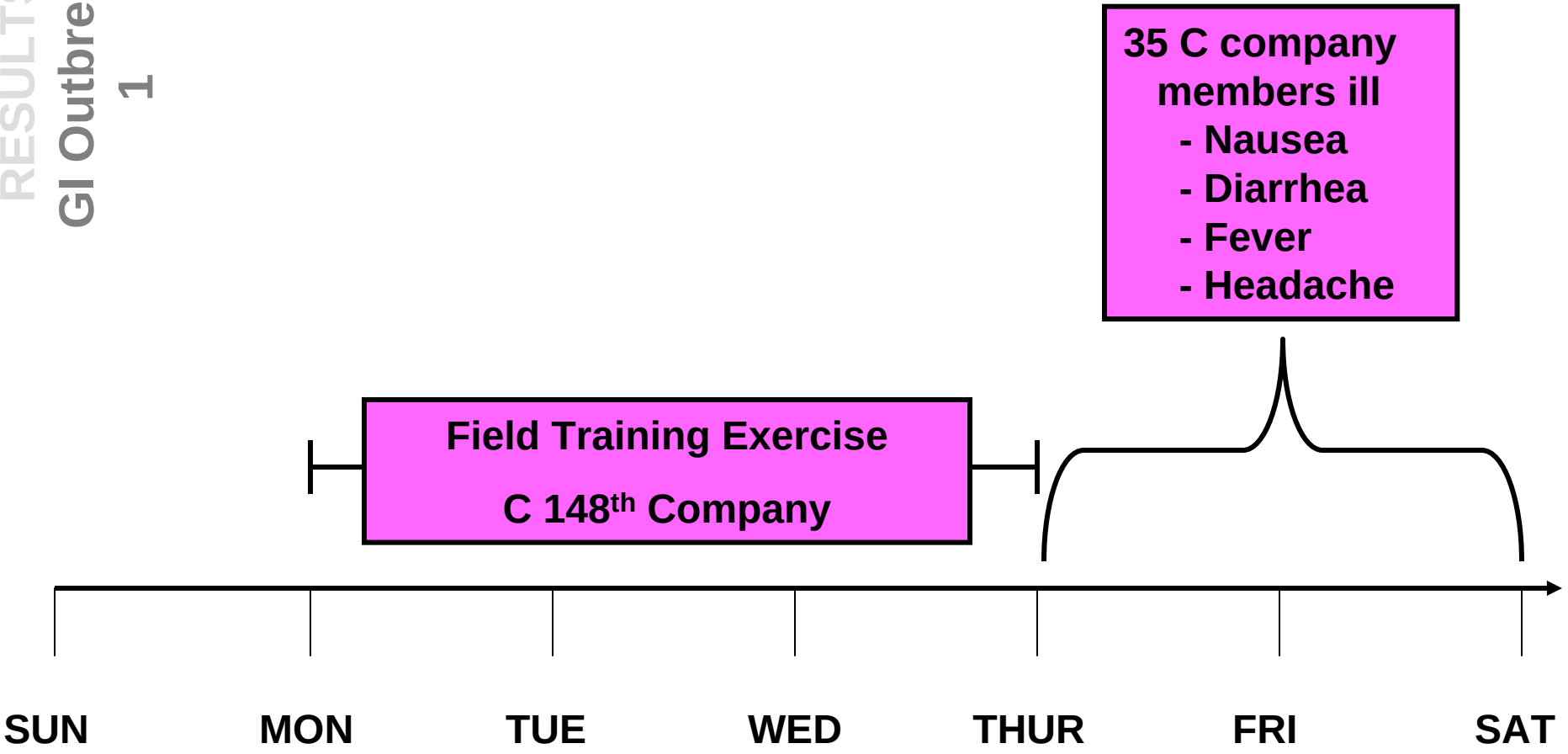
RESULTS
Outbreaks

Syndrome	No. of Outbreaks	Viral	Bacterial	Unknown
GI	21	13	2	6
RESP	7	2	4	1
Total	28	15	6	7

GI
Outbreaks

RESULTS

GI Outbreak 1

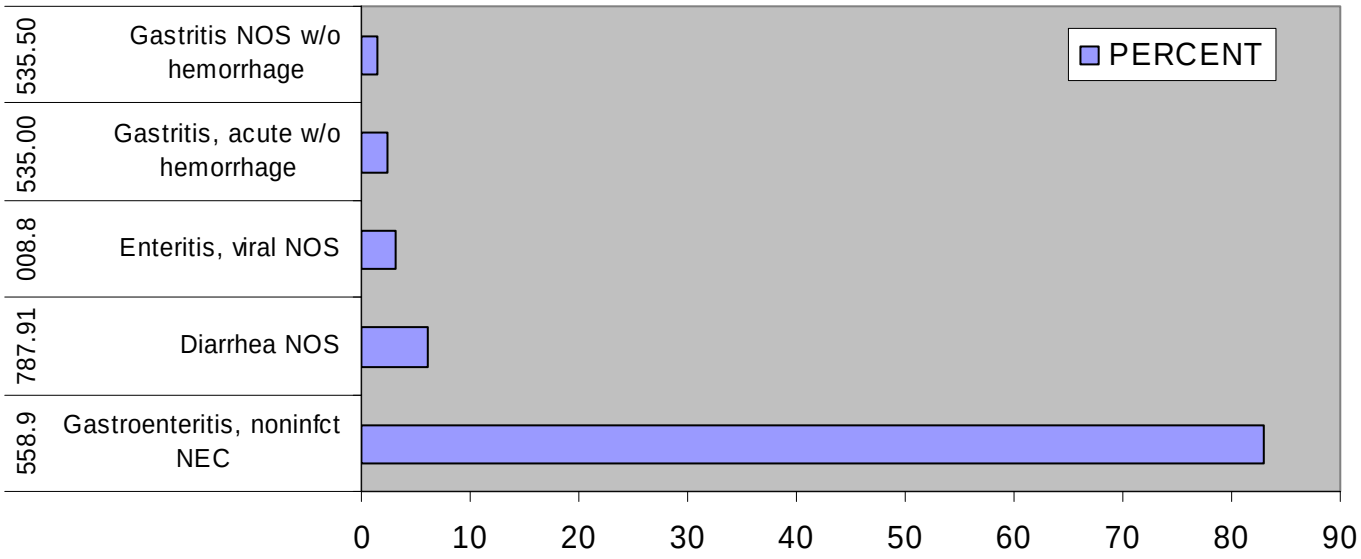


- Food and water samples from the FTX tested
  - **5/13 samples tested positive for *Campylobacter jejuni***

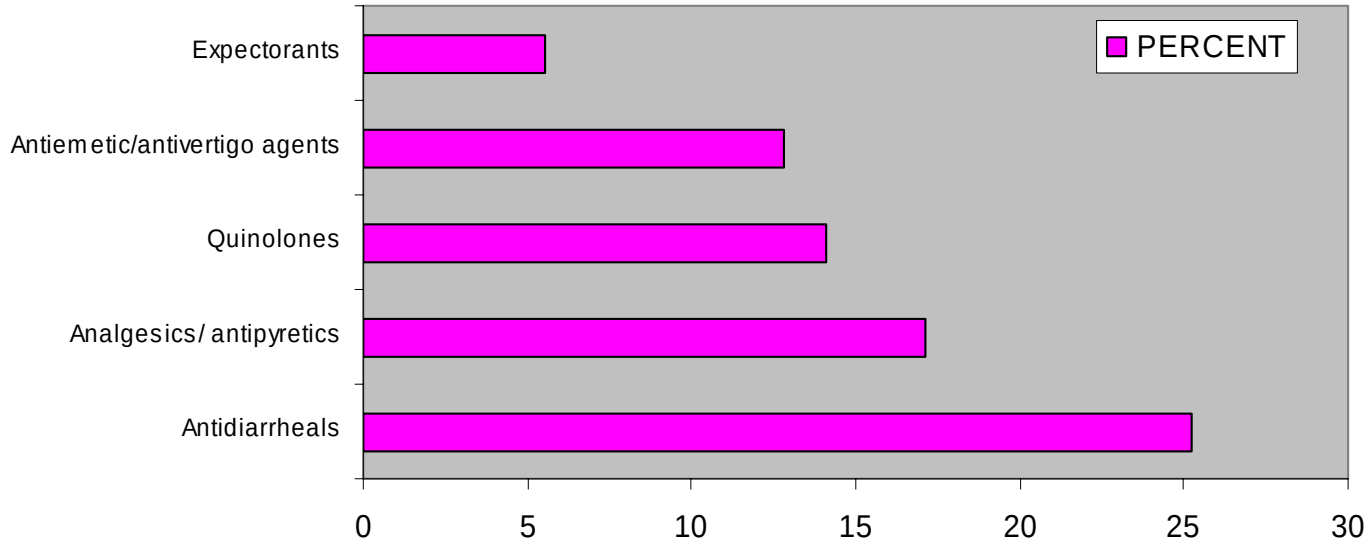
RESULTS

GI Outbreak 1

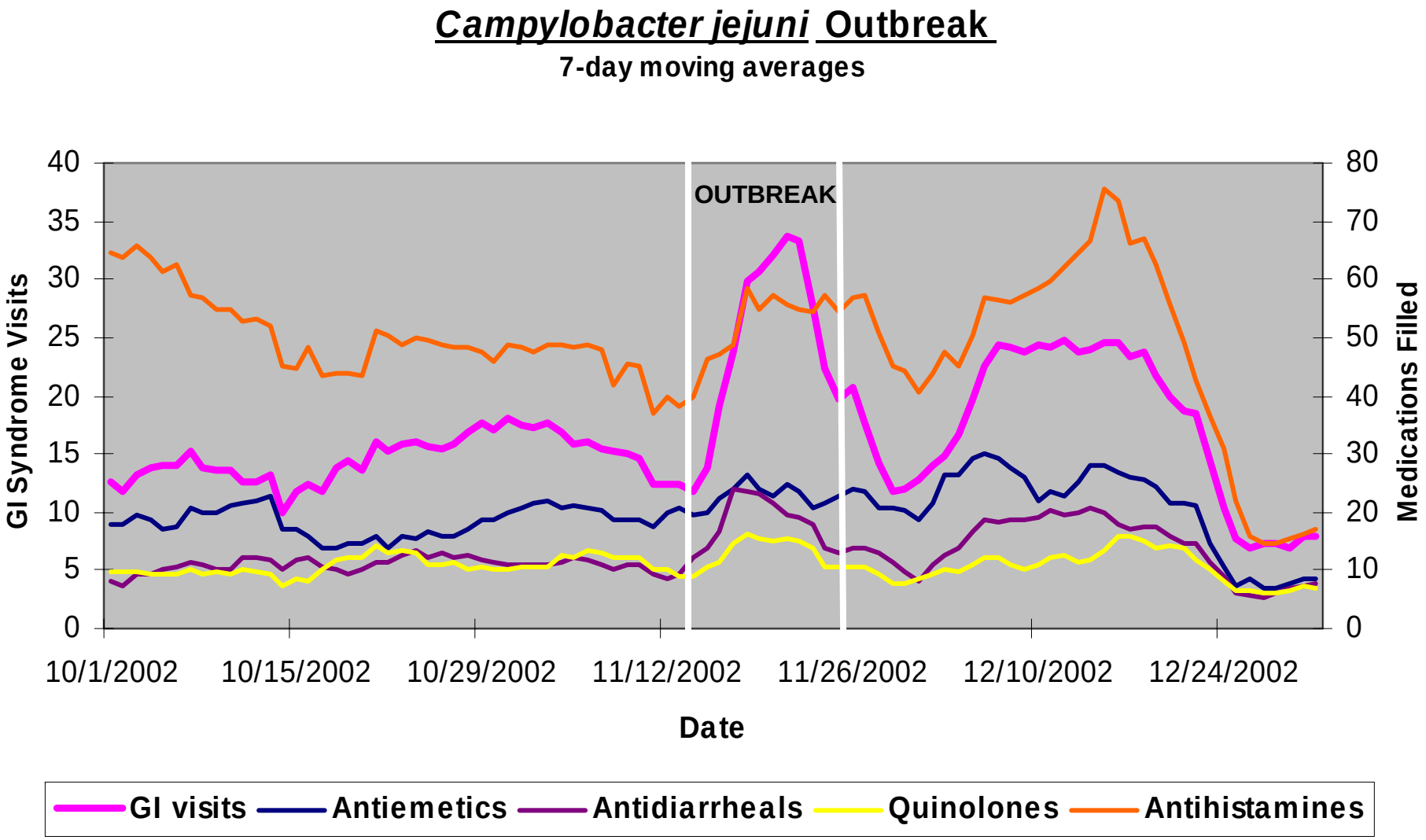
Top 5 ICD-9 codes used during a *C. jejuni* outbreak



Top 5 prescriptions written during *C. jejuni* outbreak



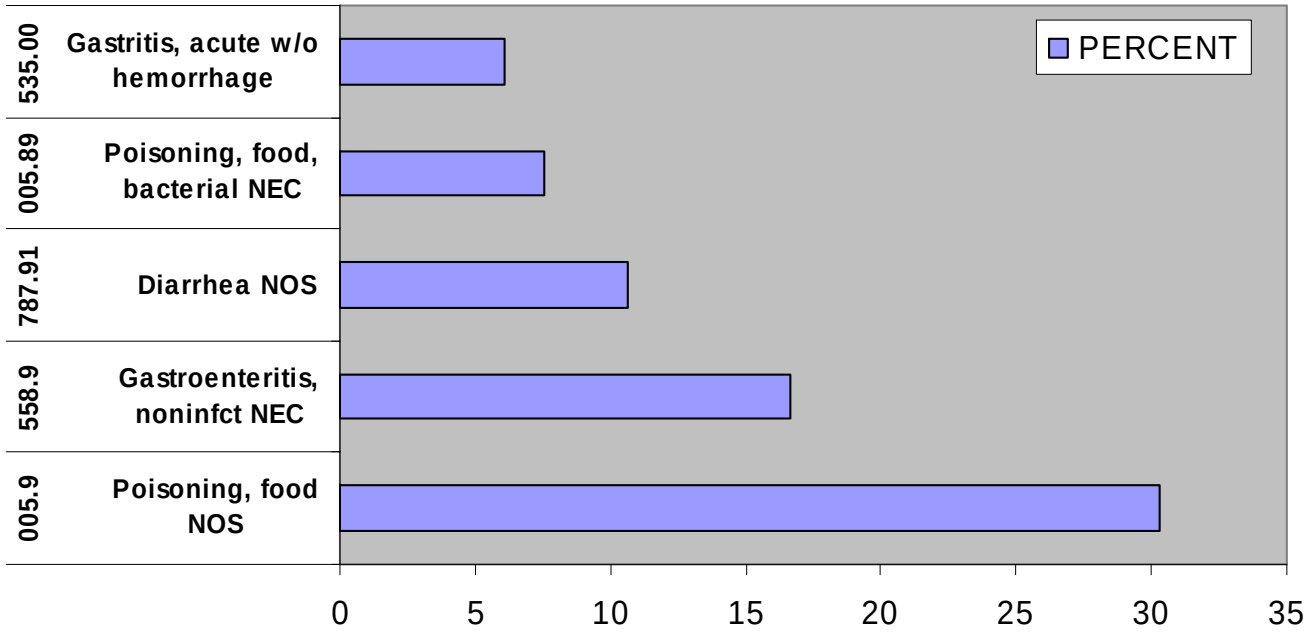
RESULTS


Campylobacter jejuni Outbreak
7-day moving averages
OUTBREAK
GI Syndrome Visits
Medications Filled
0
5
10
15
20
25
30
35
40
0
10
20
30
40
50
60
70
80
10/1/2002
10/15/2002
10/29/2002
11/12/2002
11/26/2002
12/10/2002
12/24/2002
Date
GI visits
Antiemetics
Antidiarrheals
Quinolones
Antihistamines

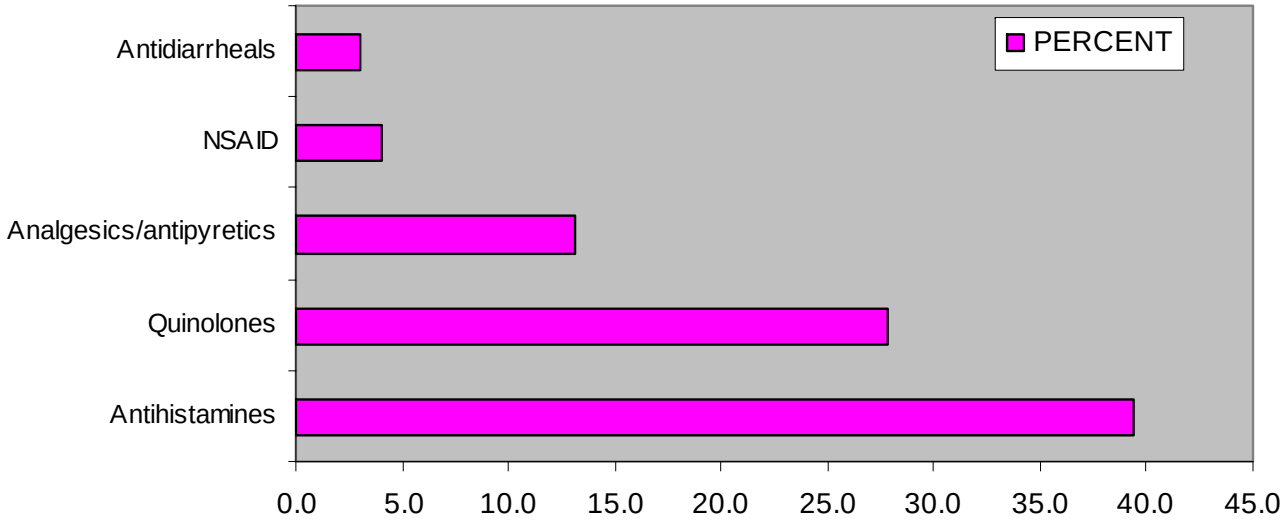
RESULTS

GI Outbreak 2

Top 5 ICD-9 codes used during a Salmonella outbreak



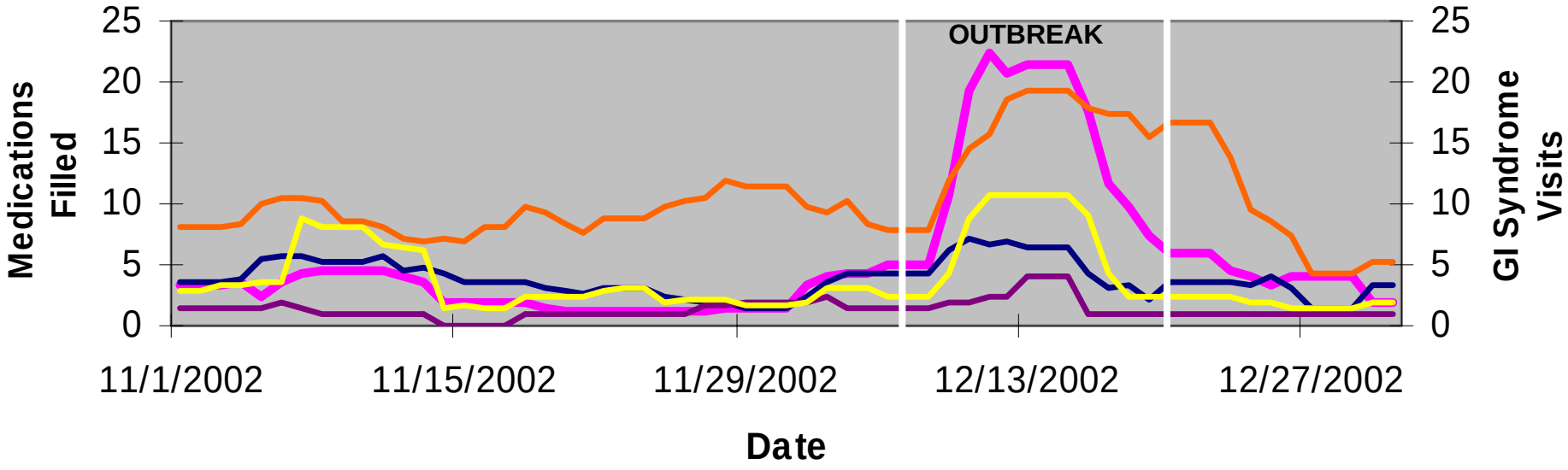
Top 5 prescriptions during the Salmonella outbreak



RESULTS

Salmonella Outbreak

7-day moving averages



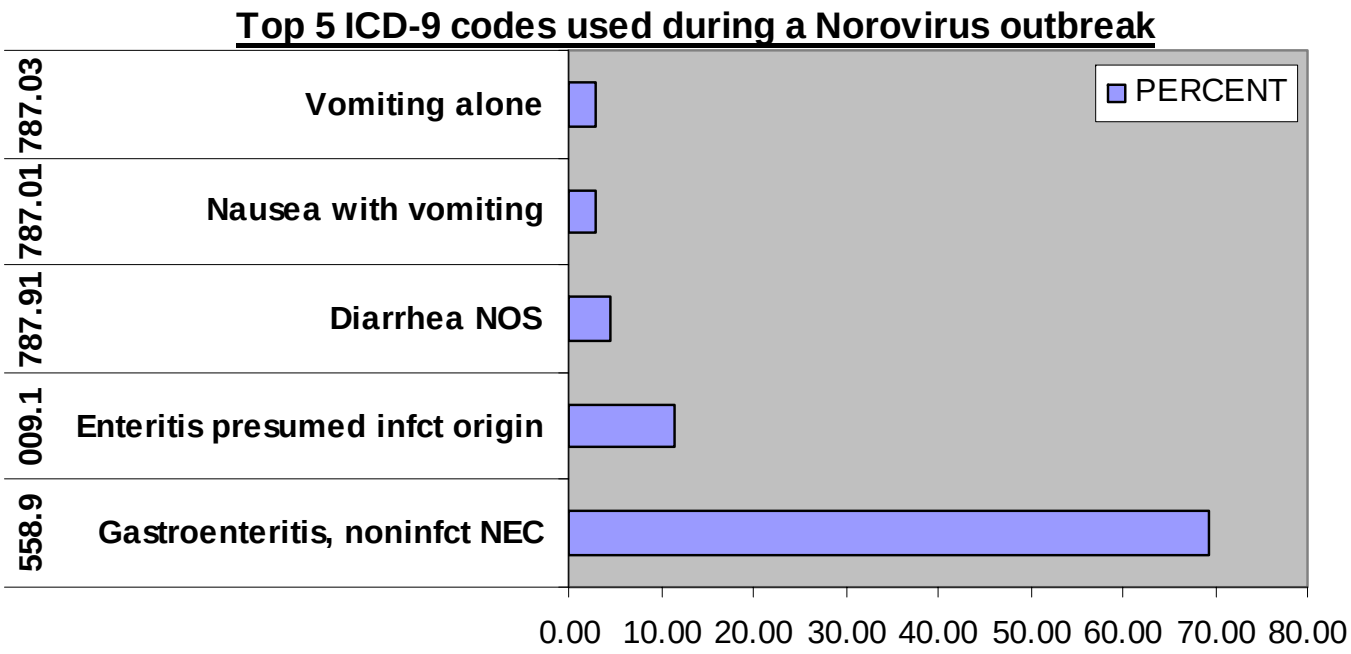
Analgesics/antipyretics: Acetaminophen, Tylenol, etc.
Antidiarrheals: Loperamide, Imodium, Pepto-bismol, etc.
Antihistamines: Includes Phenergan, Promethazine (antiemetics)
Quinolones: Ciprofloxacin, Levaquin, etc.

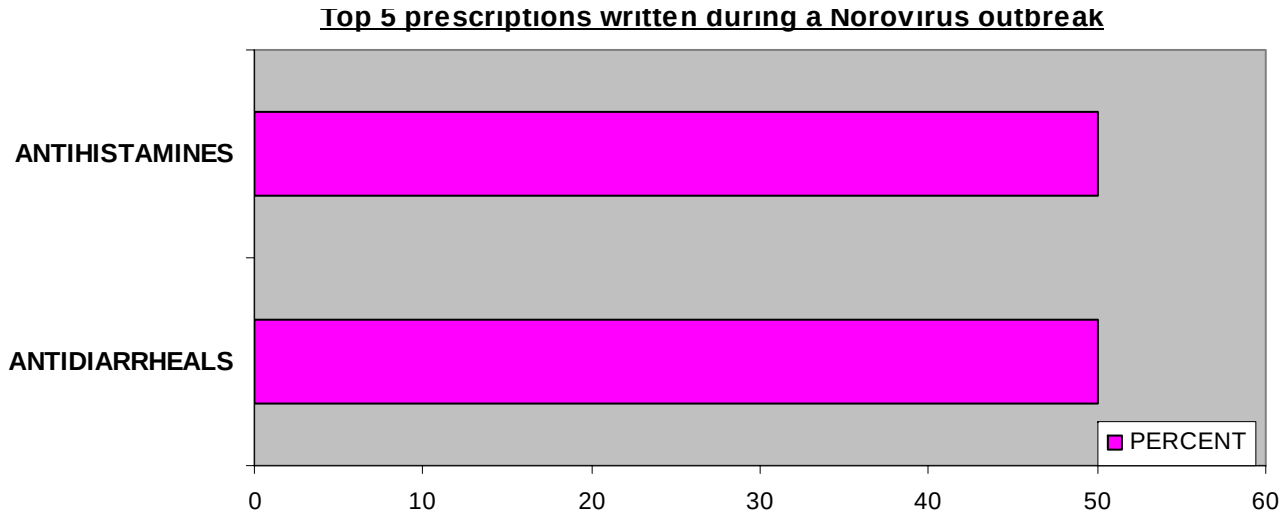
RESULTS
GI OUTBREAK 3

- At a U.S. Air Force training base in Texas[3]
  - Norovirus outbreak
  - In all 464 trainees affected
  - Lasted 7 days
  - 7/7 stool samples tested positive for Norovirus

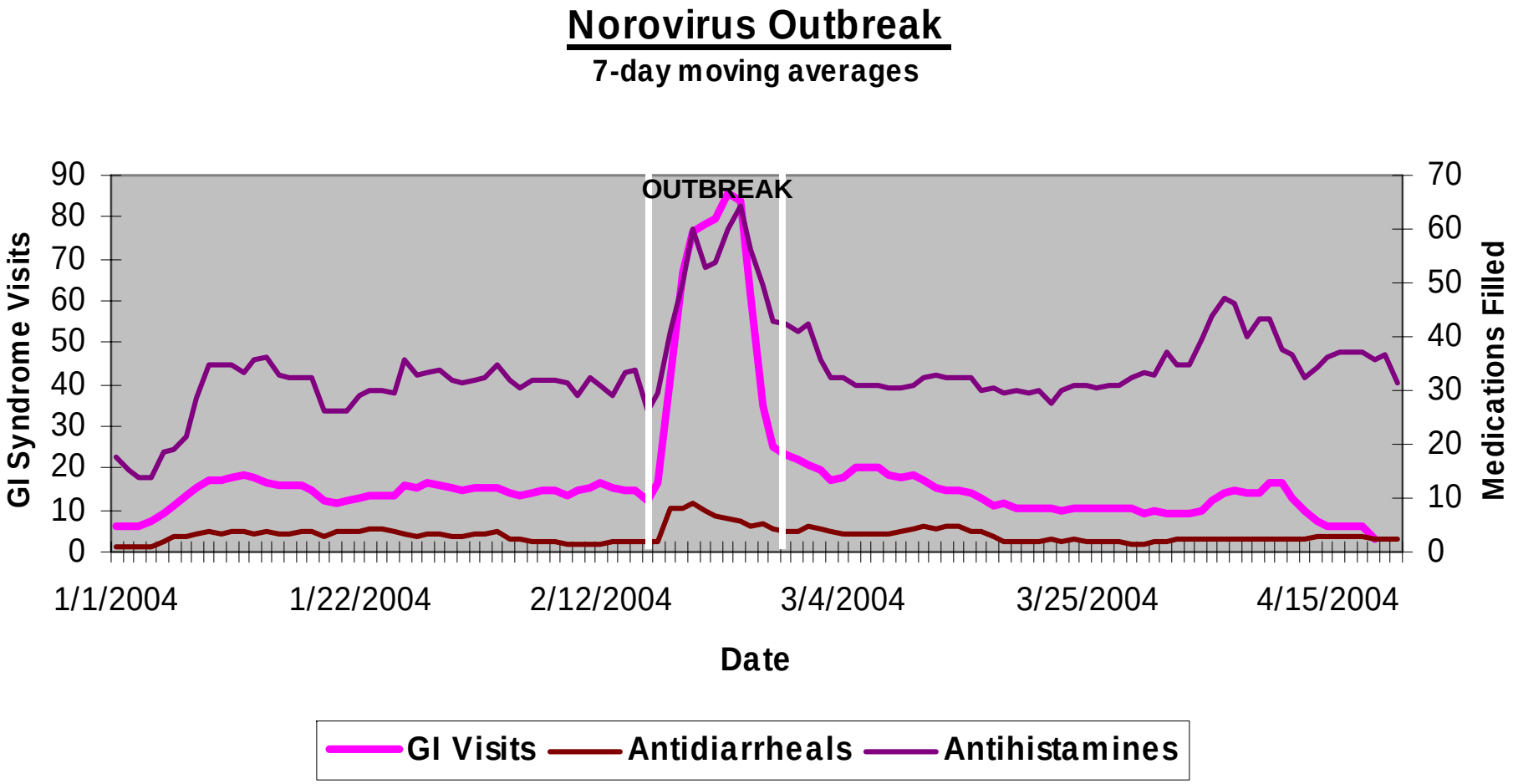
RESULTS

GI Outbreak 3





RESULTS


Norovirus Outbreak
7-day moving averages
OUTBREAK
GI Syndrome Visits
Medications Filled
90
80
70
60
50
40
30
20
10
0
70
60
50
40
30
20
10
0
1/1/2004
1/22/2004
2/12/2004
3/4/2004
3/25/2004
4/15/2004
Date
GI Visits
Antidiarrheals
Antihistamines

RESP
Outbreaks

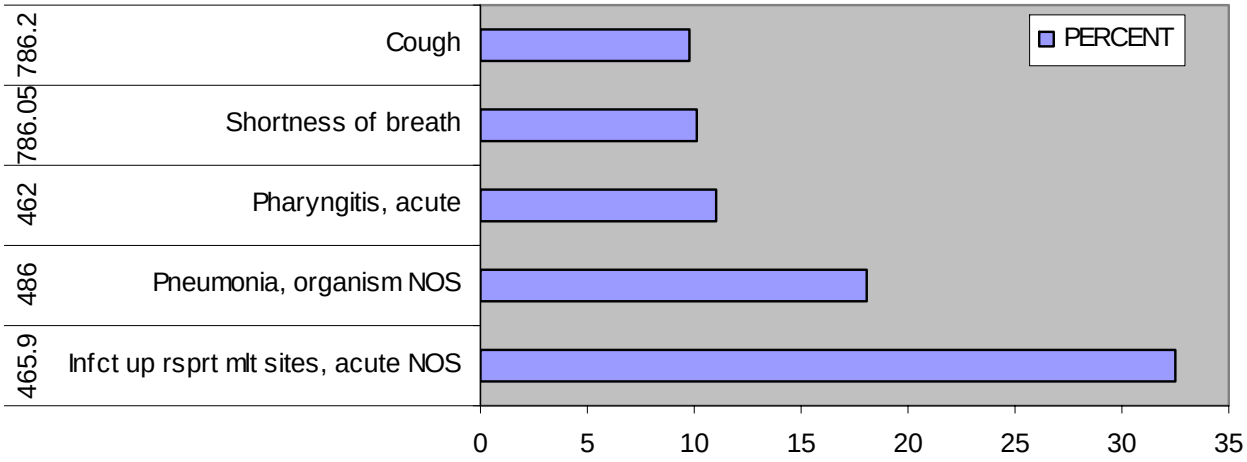
RESULTS
RESP OUTBREAK 1

- At the Marine Corps Recruit Depot in San Diego[3]
  - Largest Group A Streptococcus outbreak since 1968
  - 160 recruits admitted for pneumonia (radiographically confirmed)
  - November 1 – December 20
  - Sputum, blood and throat cultures
    - Group A Streptococcus isolated

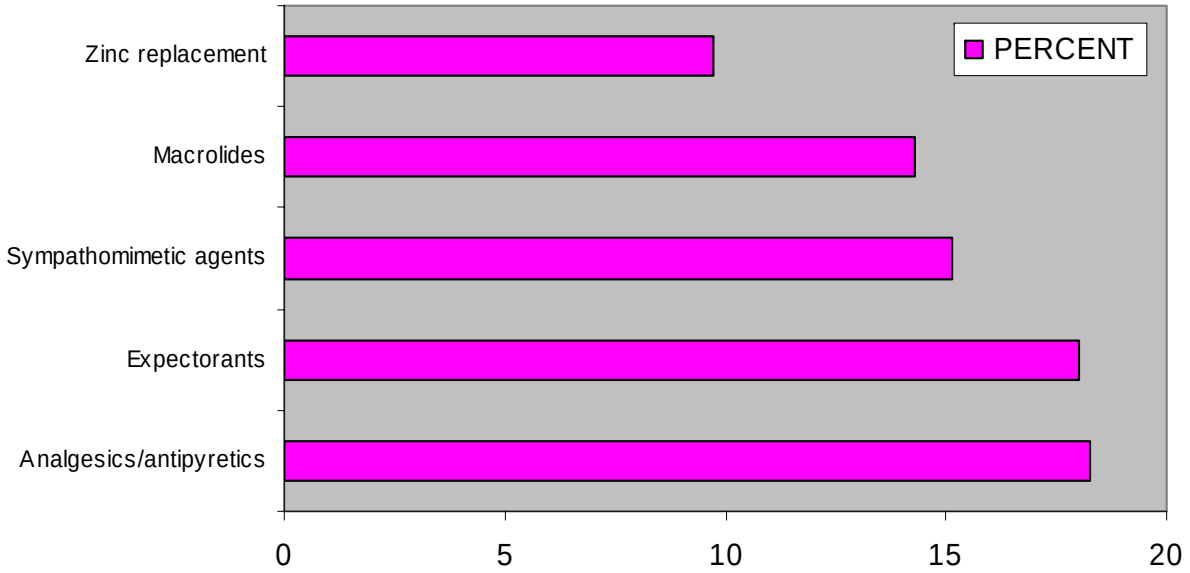
RESULTS

RESP Outbreak 1[2]

Top 5 ICD-9 codes used during a Streptococcus A outbreak



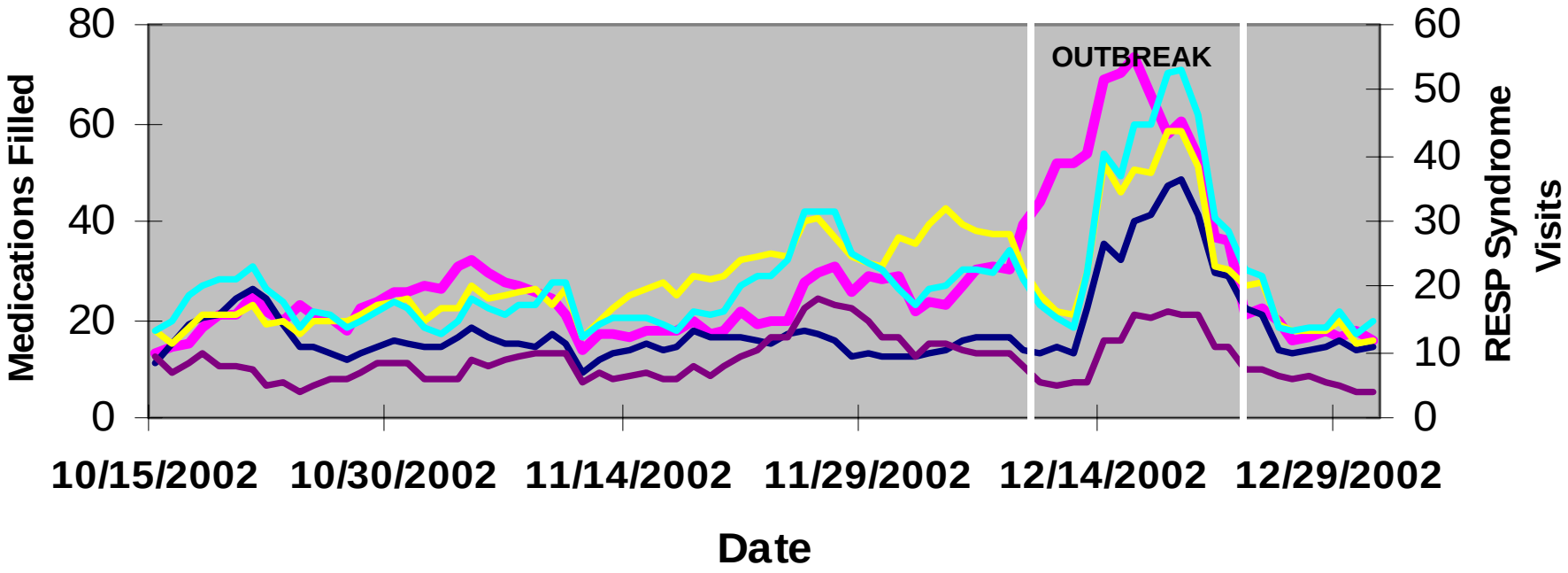
Top 5 prescriptions written during a Streptococcus A outbreak



RESULTS

Streptococcus A Outbreak

7-day moving averages



Expectorants: Robitussin, Guaifenesin, etc.

Sympathomimetic agents: Sudafed, etc

Zinc replacement: Cepacol Cold Care, etc.

Analgesics/antipyretics: Acetaminophen, Tylenol, etc.

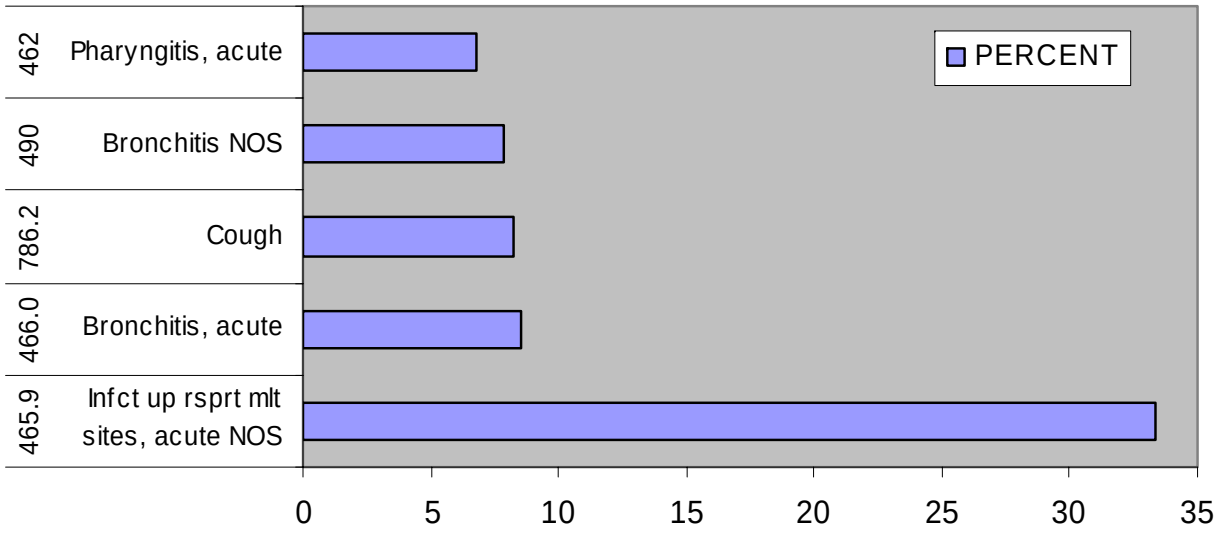
RESULTS
RESP OUTBREAK 2

- Influenza in an Advanced Individual Training population in VA in November, 2003
  - Approx. 187 cases total
  - Oct. 31st – Nov. 7th
  - Rapid flu tests positive; 5 CDC viral cultures Flu A positive, subtyped Korea-like or Fujian-like viruses

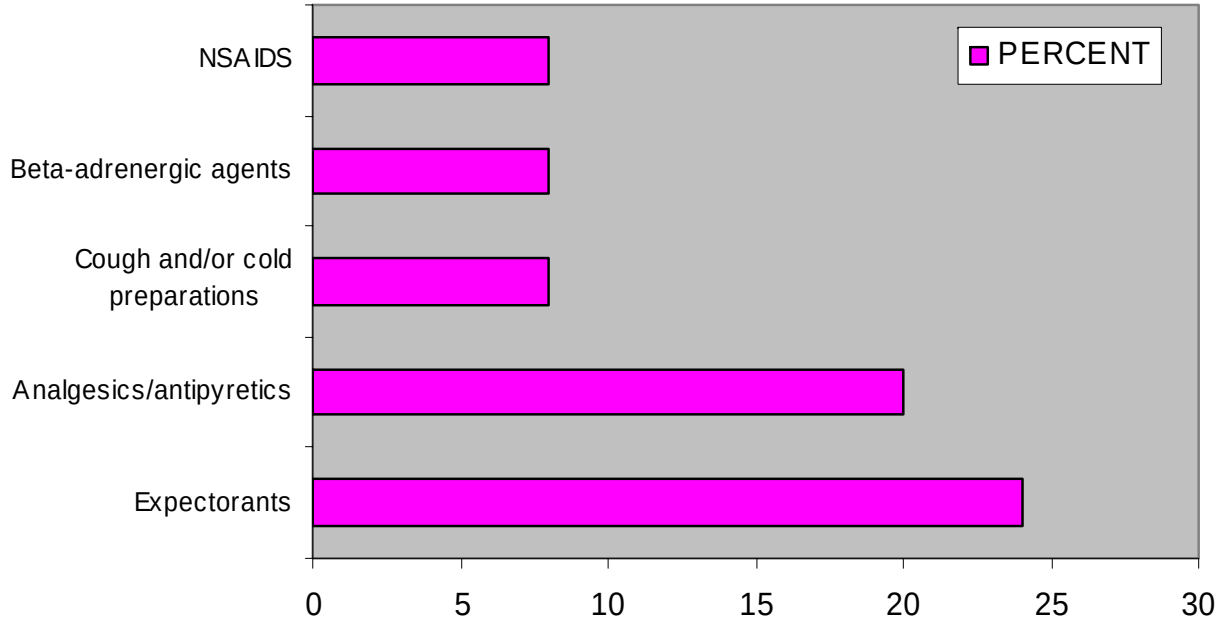
RESULTS

RESP Outbreak 2

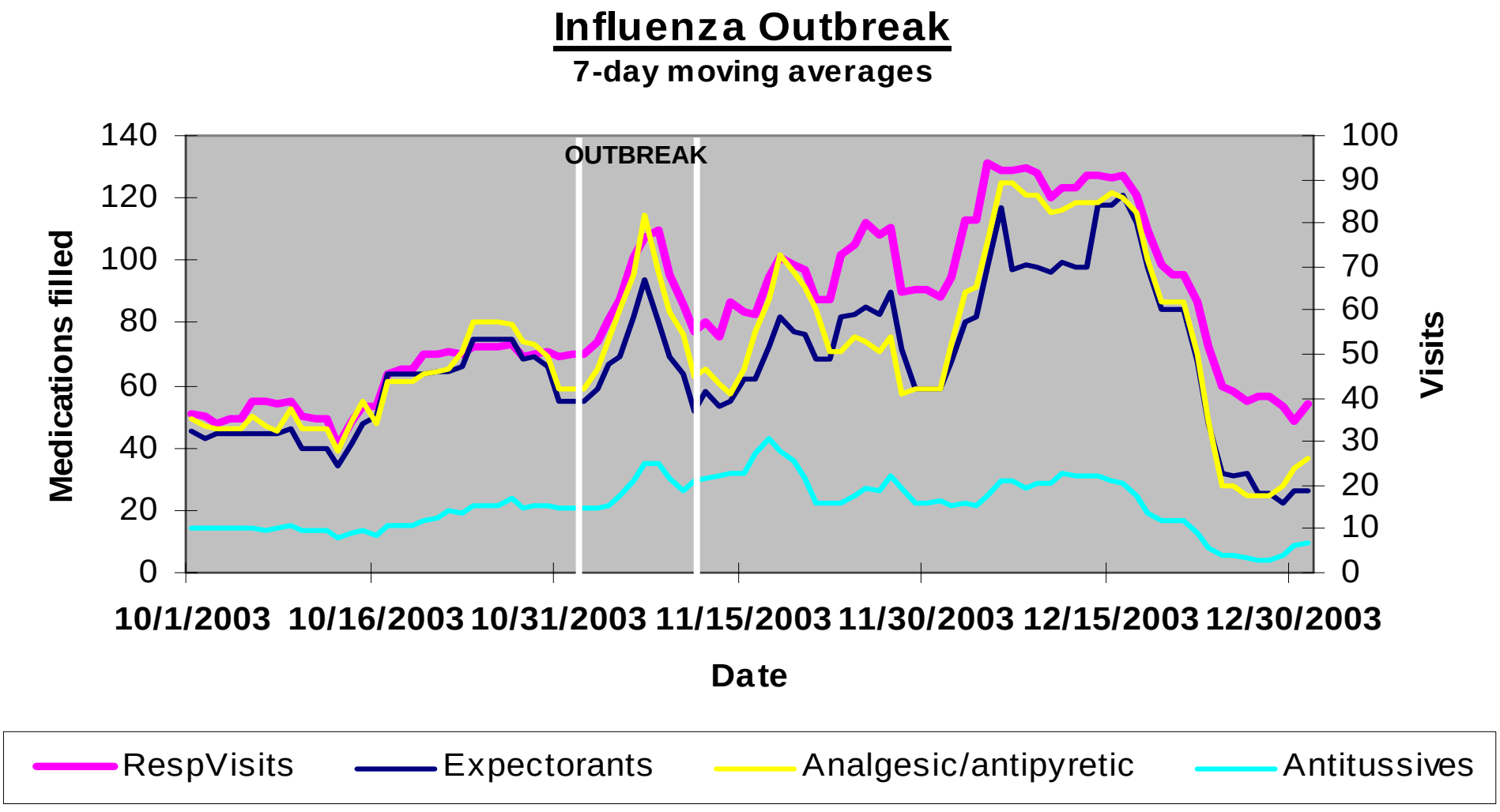
Top 5 ICD-9 codes used during an influenza outbreak



Top 5 prescriptions written during an influenza outbreak



RESULTS


Influenza Outbreak
7-day moving averages
OUTBREAK
Medications filled
Visits
140
120
100
80
60
40
20
0
100
90
80
70
60
50
40
30
20
10
0
10/1/2003
10/16/2003
10/31/2003
11/15/2003
11/30/2003
12/15/2003
12/30/2003
Date
RespVisits
Expectorants
Analgesic/antipyretic
Antitussives

RESULTS

GI group

1. Antiemetics
2. Antidiarrheals
3. Antihistamines
4. Analgesics/antipyretics
5. Antispasmodics
6. Antacids
7. Quinolones
8. Intestinal adsorbents and protectives
9. Penicillins
10. Absorbable sulfonamides

RESP group

1. Expectorants
2. Cough and/or cold preparations
3. Analgesics/antipyretics
4. Antitussives, non-narcotic
5. Sympathomimetic agents
6. NSAIDS
7. Macrolides
8. Quinolones
9. Zinc replacement
10. Penicillins

STUDY OBJECTIVES

1) Determine medications commonly prescribed for GI and Respiratory (RESP) syndromes

2) Examine trends in daily counts of medications for GI, RESP, Asthma visits during outbreaks

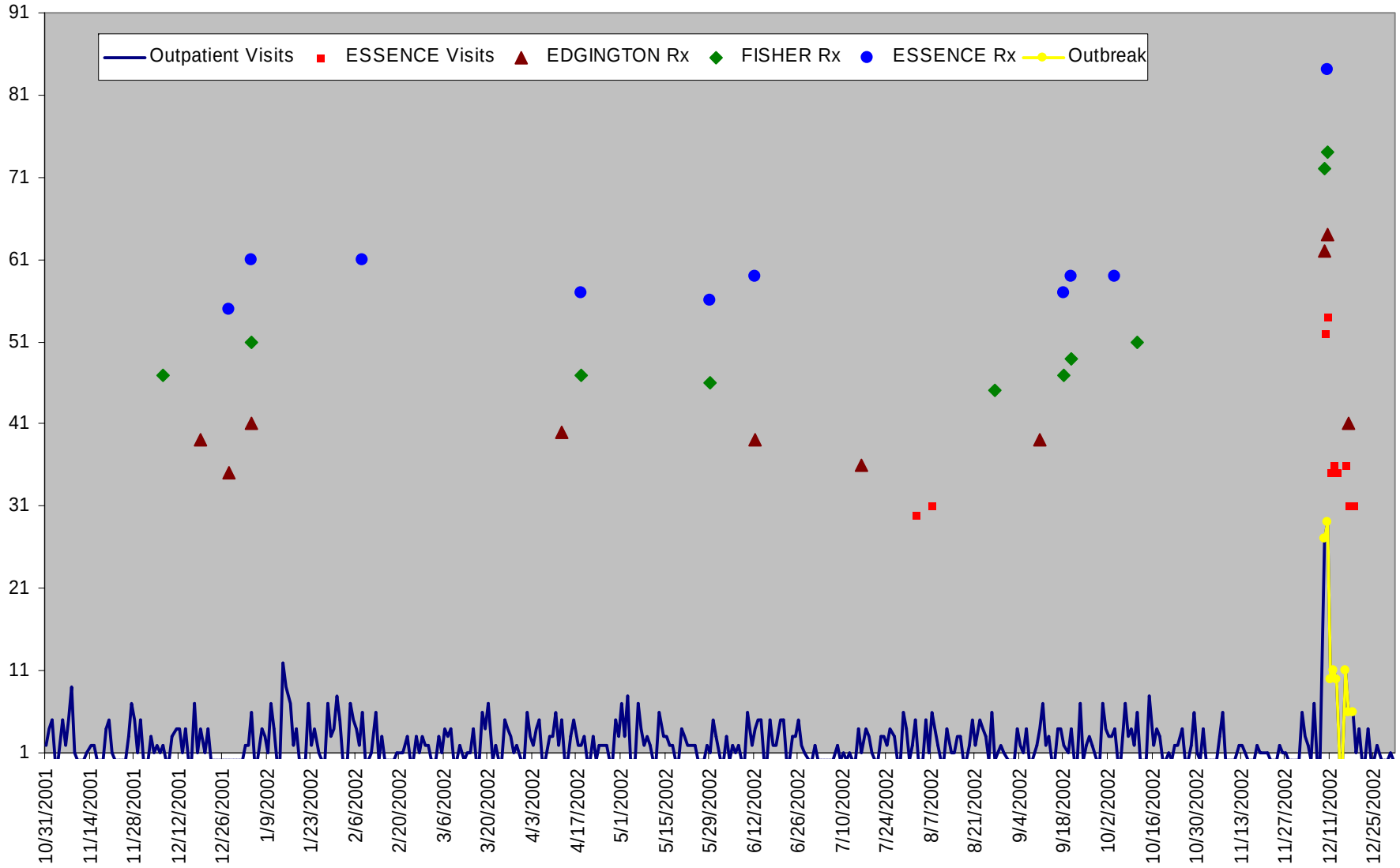
3) Conduct retrospective surveillance on GI and RESP syndrome drug groups and GI and RESP outpatient visits at installations where outbreaks occurred

METHODS

- Retrospective surveillance conducted on pharmacy and outpatient visit data for approx. 1 year prior to and including the outbreak timeframe
  - Regression/Exponential Weighted Moving Average (EWMA) detection algorithms run on daily total GI/RESP visits, daily total PDTS syndrome groups and each GC3 group → output of p-values
  - P-values from individual larger count GC3 groups (>1 prescription in 3 days) were combined using Fisher and Edgington combination p-value methods
    - More information on combination p-value methods → Dr. Howard Burkom's talk at 2:00 p.m.
  - Detections with approximately 1 per 6 weeks false alert rate were identified graphically

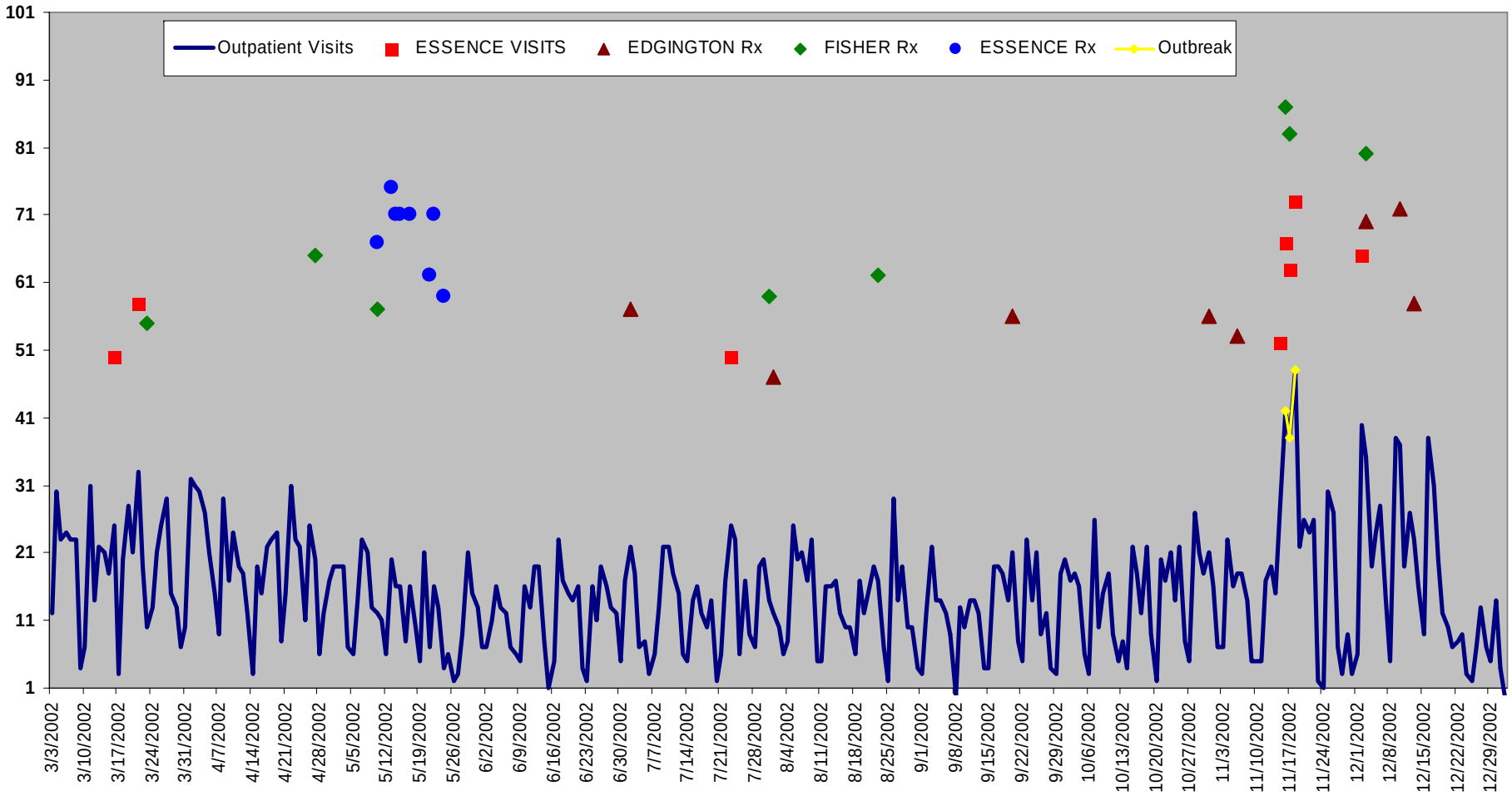
Salmonella Outbreak

(12/9/02 to 12/18/02)



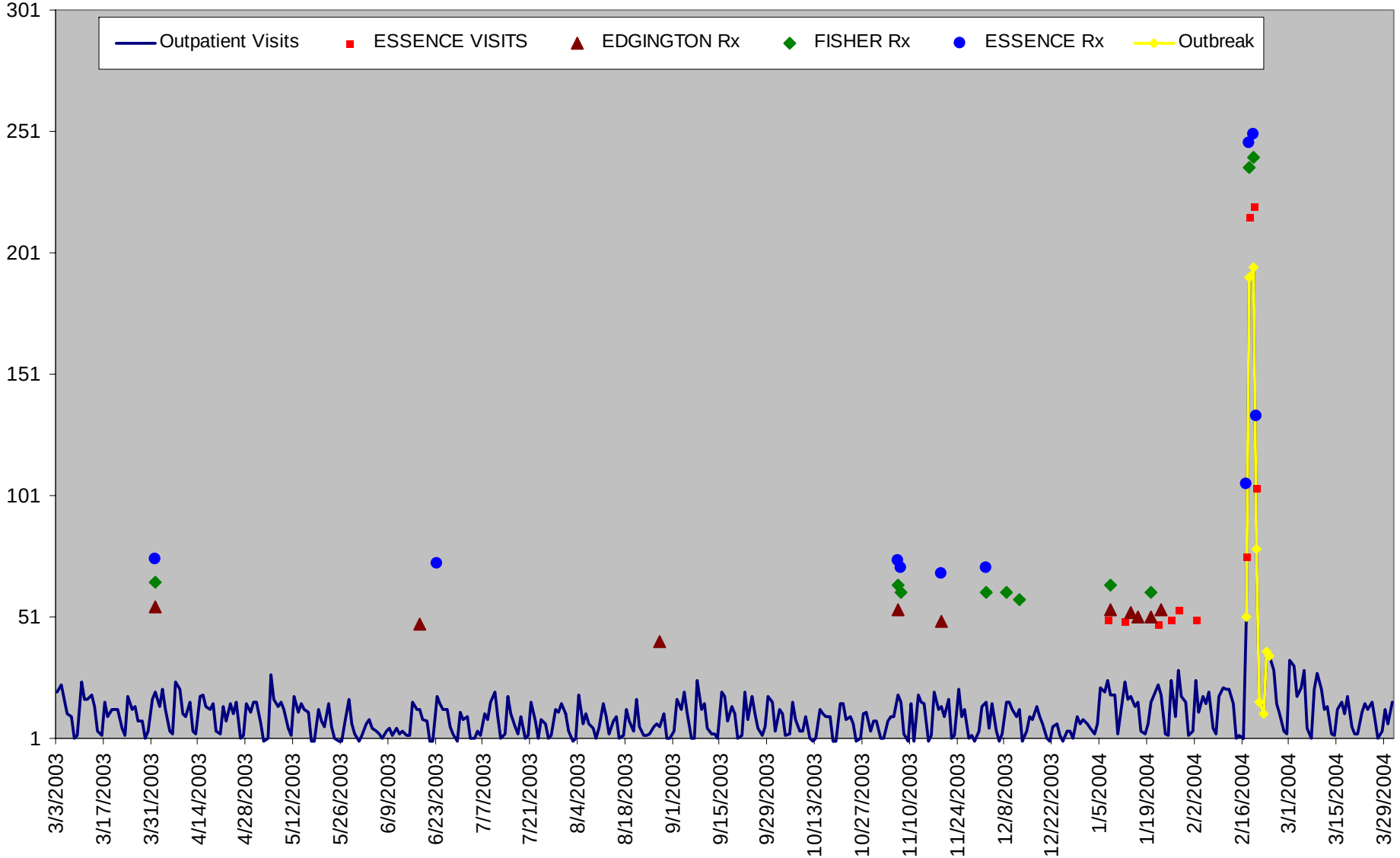
C. jejuni Outbreak

(11/16/02 – 11/18/02)



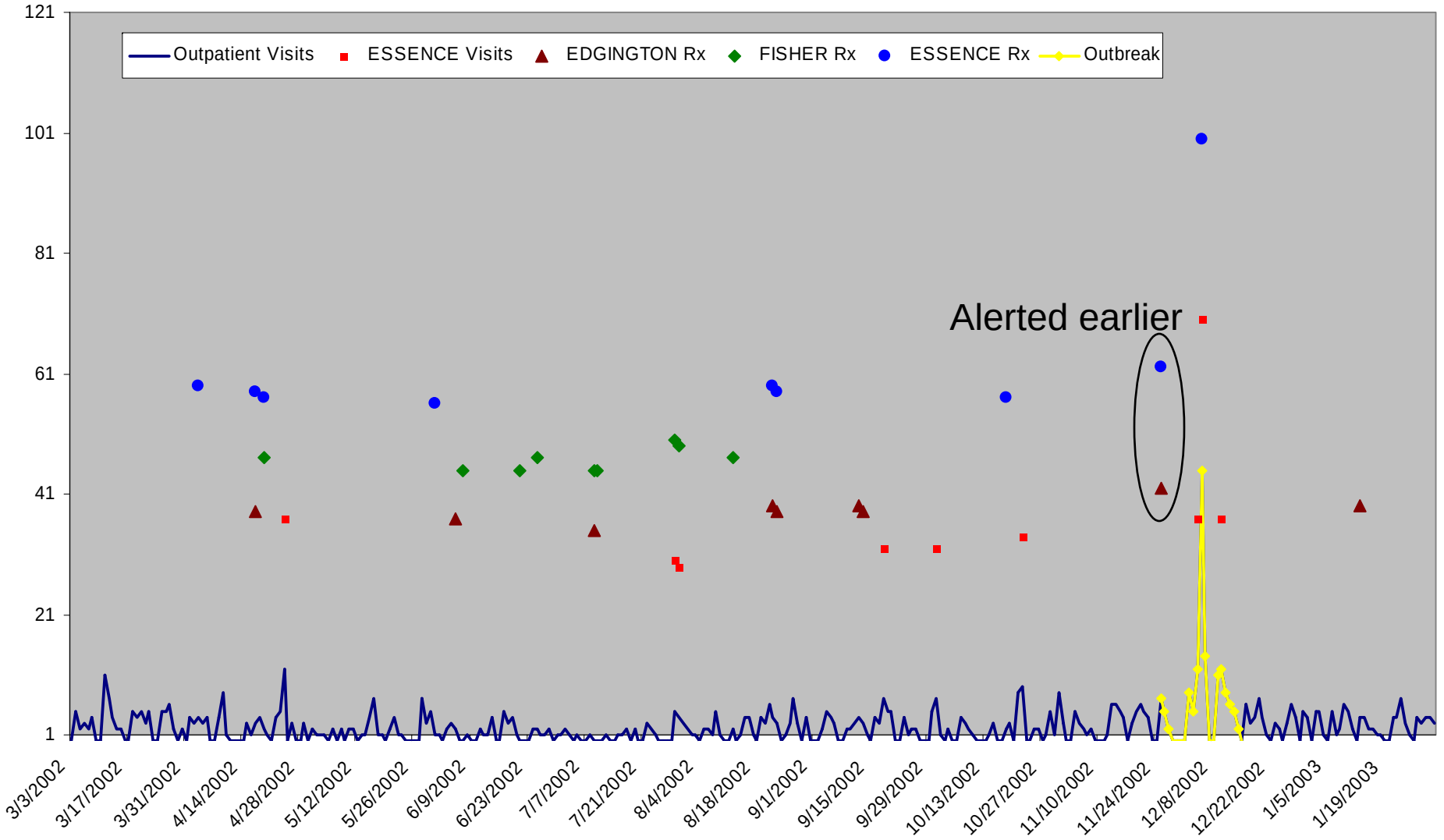
Norovirus Outbreak[3]

(02/17/04 to 02/24/04)



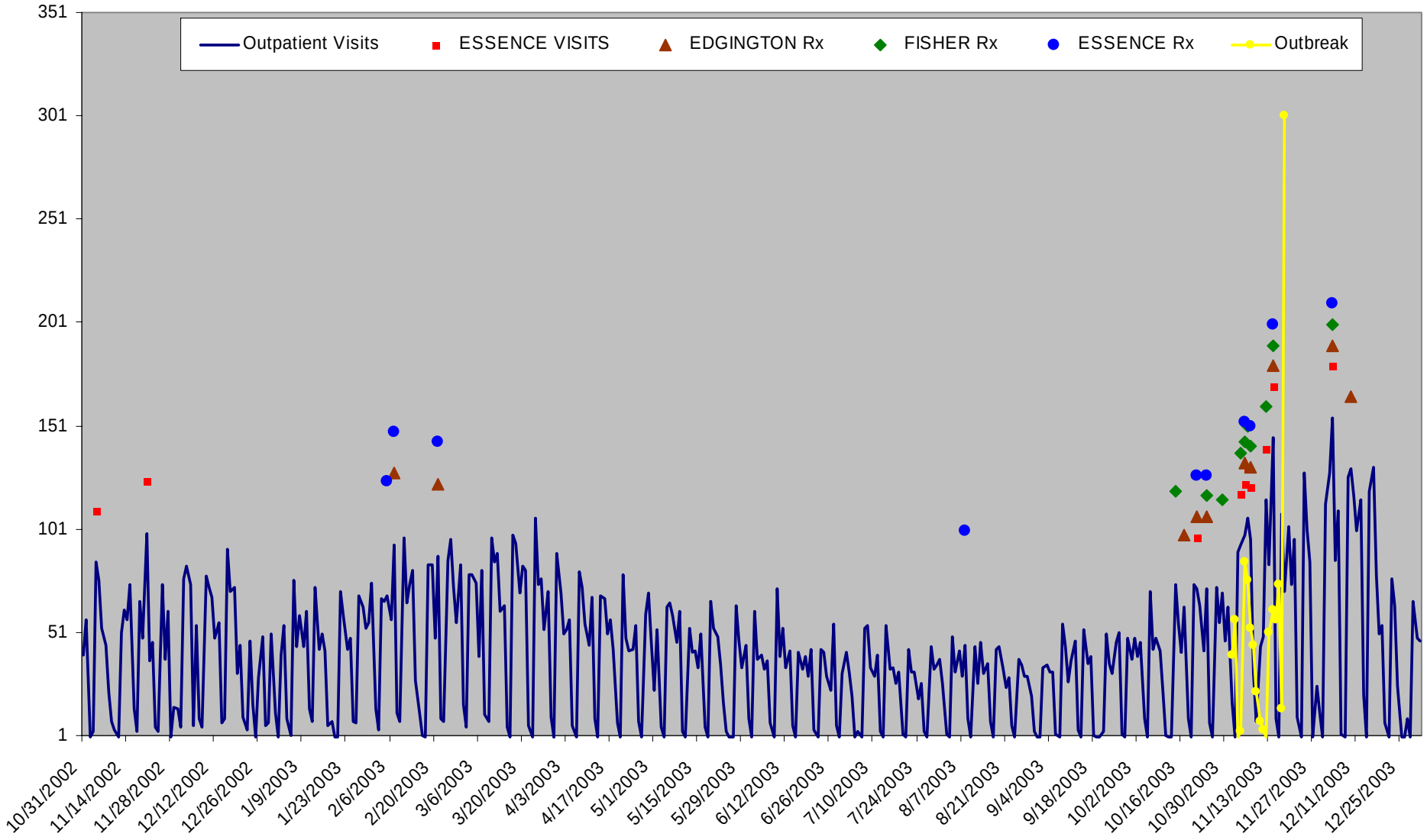
Norovirus Outbreak

(11/25/02 to 12/15/02)



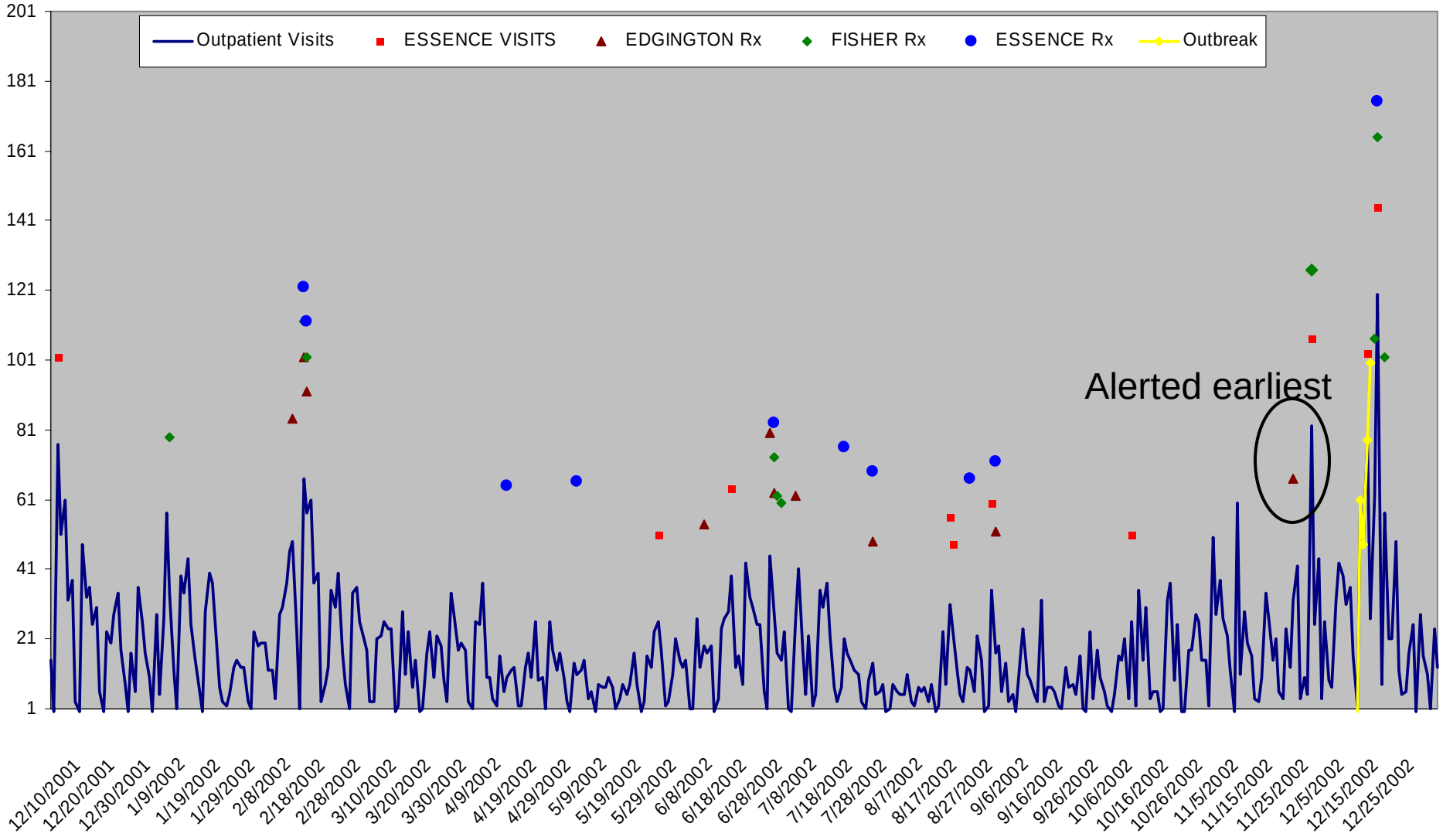
Influenza Outbreak

(11/1/03 to 11/18/03)



Group A Streptococcus Outbreak

12/08/02 to 12/12/02



CONCLUSIONS

- Use of the GC3 classification system in military pharmacy data can increase sensitivity without significantly affecting the false alert rate.
  - A limitation: Certain medications were found in more than one GC3 group. If these don't contribute to an outbreak, the signal is weakened

- Outbreaks were characterized by increases in certain GC3 groups and combinations of GC3 groups but these varied by outbreak type.

- Syndromic drug groups were formed using medications more commonly used during outbreaks, increasing the overall sensitivity of the system.

CONCLUSIONS

- The ESSENCE outpatient visit detector, the gold standard, alerted for all 6 outbreaks.
- The ESSENCE pharmacy detector performed well and alerted for 5/6 outbreaks.
- The two p-value combination methods have distinct advantages. The Fisher method alerted for 5/6 outbreaks and was more sensitive to individual GC3 increases. Whereas, the Edgington method alerted for 3/6 outbreaks but was more responsive to consensus and in 2 outbreaks alerted earlier.
- Combination methods are more sensitive and specific if low count gc3 streams are accumulated or dropped.

FUTURE RESEARCH

- Investigate performance of algorithms for other outbreaks
- Investigate performance of detectors for a GC3 group switch, i.e., ignore product groups that don't meet a certain minimum count
- Continue to investigate product groups that give more signal and less noise
- Prospective surveillance using ESSENCE pharmacy and combination method detectors

REFERENCES

1. http://www.pec.ha.osd.mil/ICD/ICD_MTF_040502.doc

2. Centers for Disease Control and Prevention. *Outbreak of group A streptococcal pneumonia among Marine Corps recruits – California, November 1 – December 20, 2002.* MMWR. 2003;52(6):106-109.

3. Yamane, GK, Shibukawa-Kent, RL. 2004. *A large norovirus GI outbreak among trainees at a USAF training base.* Seventh Annual Force Health Protection Conference, Aug. 8-12, 2004.

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THANK YOU
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ATTENTION